

**SB**  
**SmithKline Beecham**  
*Pharmaceuticals*

4 3 5 7 '00 NOV 15 A9:11

November 14, 2000

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

Re: Docket No. **00D-1424**; Draft Guidance for Industry on  
Analytical Procedures and Method Validations:  
Chemistry, Manufacturing and Controls  
Documentation  
Federal Register, August 30, 2000 (65FR169)

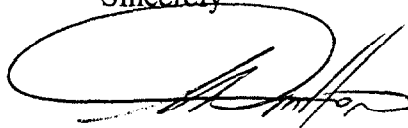
Dear Sir/Madam:

The draft guidance, according to the Notice issued at the time of the publication is intended to provide recommendations to applicants on submitting analytical procedures, validation data and samples to support the identity, strength, quality, purity and potency of drug substances and drug products.

Provided herein, are detailed specific comments on the aforementioned draft guidance.

SmithKline Beecham welcomes the opportunity to work with FDA and industry in crafting improved versions of this draft guidance.

Sincerely



Thomas M. Hogan  
Director  
North America Regulatory Affairs

Attachment

00D-1424

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**FDA Guidance for Industry for public comment:  
Analytical Procedures and Methods Validation - Chemistry, Manufacturing, and Controls  
Documentation**

Posted: 8/30/2000, Publish Date: 8/30/2000

**SB Pharmaceutical Technologies Comments**

Section	Guidance Line (or page #)	Comment	Rationale
III	114	Remove requirement to provide comparative data with regulatory procedure for an alternative analytical procedure	<p>It is not always possible to run the regulatory method due to difficulty in reproducing satisfactory experimental conditions; this is often the reason that an alternative method is developed.</p> <p>If an alternative analytical procedure has been fully validated it should stand on its own.</p>
VI	324	Insert 'where known' before 'the type of impurity'	It may not be possible to unequivocally identify the source of all chromatographic peaks.
VII	419, 420	Relocate paragraph to separate section on 'Supporting Data for Regulatory Filings'	Method validations are working documents; inclusion of a lot of supporting data will make them unwieldy for daily use

*SB Pharmaceutical Technologies comments on FDA Guidance for Industry:  
Analytical Procedures and Methods Validation - Chemistry, Manufacturing, and Controls Documentation*

Section	Guidance Line (or page #)	Comment	Rationale
VII	450 - 453	Relocate paragraph to separate section on 'Supporting Data for Regulatory Filings'	Method validations are working documents; inclusion of a lot of supporting data will make them unwieldy for daily use
VII	498 - 514	Relocate paragraph to separate section on 'Supporting Data for Regulatory Filings'	Method validations are working documents; inclusion of a lot of supporting data will make them unwieldy for daily use
VII	535	Clarify wording in header to table for Assay Dissolution Measurement etc	It is not clear whether the column header refers to Dissolution Assay and Content/Potency, or Assay, Dissolution and Content/Potency
VII	535	Delete column for Specific Tests	All recommended tests are qualified by the subscript 'may be needed in some cases' which gives no clear guidance as to whether they should or should not be undertaken
XI	814	Add a sentence 'Unless a specific column manufacturer is specified.' after '...analytical procedure description.'	Defining a specific column manufacturer automatically defines the column construction
XI	1044	Remove	Not necessary to include the rationale for selection of the dissolution medium in the method and validation. The rationale will be discussed in the Dev Pharmaceuticals section of the filing.

*SB Pharmaceutical Technologies comments on FDA Guidance for Industry:  
Analytical Procedures and Methods Validation - Chemistry, Manufacturing, and Controls Documentation*

Section	Guidance Line (or page #)	Comment	Rationale
XI	1059	Remove	The method may be used for more than one sample type with different acceptance criteria. These are normally defined separately from the method in specifications or protocols.
XI	1061	Add 'and/or calibration testing' after 'system suitability criteria'	To cover the use of spectroscopic methods of analysis and to make it consistent with the recommendations of section XI C.
XI	1068	Clarify wording of this sentence.	The sentence is ambiguous. It is not clear whether it is referring to completion of the dissolution test or to the subsequent analysis or to both.



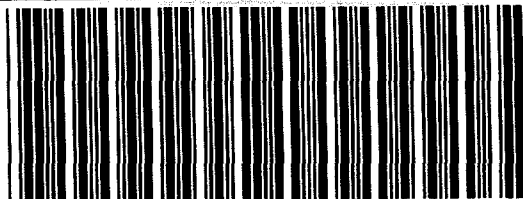
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### About our Terms and Conditions

#### 1. DHL's Contract with you:

These terms and conditions, along with those set out in our Worldwide Express Guide, are all the terms of the contract between you, the sender of the shipment, and us, DHL. When you tender a shipment to us, you accept our terms for you, the sender and for anyone else who has an expressed interest in the shipment. Our terms and conditions also protect anyone who may contract to collect, transport or deliver your shipment. No employee of DHL or anyone else has the authority to change any of our terms or conditions, or make any promises on our behalf. The terms and conditions of this airbill shall govern in the event of any inconsistencies that might exist in any other transportation documents accompanying this shipment.

#### 2. What shipment means:

A shipment means all documents or parcels that travel under one airway bill, not just any single document or envelope included in a shipment. You certify that the shipment details are complete and accurate. You agree that all shipments may be carried by any means, including air, road or any other carrier unless you give us specific instructions to the contrary.

#### 3. International Shipments:

You appoint DHL as your agent to conduct Customs entry and clearance and certify DHL as your consignee solely for the purpose of designating DHL as your Customs Broker to perform Customs entry and clearance.

#### 4. Shipments we do not accept:

We do not accept as a shipment anything that is considered a restricted article or hazardous material by the Department of Transportation (DOT), International Air Transport Association (IATA), or the International Civil Aviation Organization (ICAO).

We do not accept any shipments that contain items that we cannot transport legally or safely, including, but not limited to:

- |          |                                 |
|----------|---------------------------------|
| Animals  | Perishables                     |
| Currency | Precious Metals                 |
| Liquor   | Precious Stones                 |
| Plants   | Negotiable Items in Bearer Form |

For full information about shipments we cannot accept for shipping, please contact your nearest DHL Service Center.

#### 5. Claims:

If you wish to submit a claim for a lost (includes misdelivered) or damaged shipment, the shipper must:  
\* Submit the claim in writing.  
\* Your claim must be received within 30 days from the date that we accept your shipment.  
\* Send or take your claim to your nearest DHL office.

Please note: We will not review a claim until all shipping and any other related charges owed have been paid to DHL.

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#### 6. Delayed Shipments:

We will make every effort to deliver your shipment according to our regular delivery schedules. DHL is not liable for any delays, even if they are our fault in:

- \*Picking up a shipment
- \*Transporting a shipment (including delays caused by diversions)
- \*Delivering a shipment

DHL reserves the right, without admitting liability, to refund transportation/shipping charges, but is not obligated to do so.

#### 7. Circumstances beyond our control:

We are not liable if a shipment is lost (includes misdelivered) or damaged because of circumstances beyond our control. These circumstances include:

- \*An "Act of God", for example an earthquake, cyclone, storm or flood
  - \*"Force Majeure" for example war, plane crash or embargo
  - \*Any defect or characteristic to do with the nature of the shipment, even if known to us when we accepted it
  - \*Any action or omission by anyone outside DHL. For example:
    - The sender of the shipment
    - The receiver
    - An interested third party
    - Customs or government officials
    - The postal service, another carrier or a third party who we contract to deliver to destinations that we do not serve directly.
- We are not liable even if the sender did not ask for or know about a third party delivery agreement.

We are also not liable for electrical or magnetic damage to, or erasure of, electronic or photographic images or recordings.

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We are not liable for the following, whether they arise in contract or any other form of civil action, including negligence, and even if they are DHL's fault:

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- \* Breach of other contracts
- \* Consequential damages or loss include, but are not limited to: lost income \* Profits \* Interest \* Markets \* Use of contents

#### We are liable for

#### 9. Extent of our liability:

Our liability for a lost or damaged shipment is limited to the lowest of these 3 amounts:

- \*US \$100, or
- \*The actual amount of the loss or damage, or
- \*The actual value of the document or parcel. This does not include any commercial utility or special value to the shipper or any other person.

#### 10. What "Actual value" means:

The lowest of the following amounts, determined as at the time and place we accepted the shipment:

- Documents** (meaning any shipment without commercial value):
  - \*The cost of replacing, reconstructing or reconstituting the documents

- Parcels** (meaning any shipment with commercial value):
  - \*The cost of replacing or replacing the parcel, or
  - \*The resale or fair market value of the parcel

The actual value of a parcel cannot be more than the original cost to you plus 10 percent.

#### Warsaw Convention

11. If the transportation of a shipment involves an ultimate destination or stop in a country other than the country of departure, the Warsaw Convention limits our liability for loss or damage to such shipment. You agree that your shipment may be carried via intermediate stopping places which we deem appropriate.

#### Shipment Insurance

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